

Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in this application:

Listing of Claims:

Claims 1-6 (Canceled)

7. (Previously presented) The monoclonal antibody of claim 33, wherein the antibody is a scFv.

8. (Previously presented) The monoclonal antibody of claim 33, wherein the antibody is a Fab.

9. (Previously presented) The monoclonal antibody of claim 33, wherein the antibody is a fully assembled antibody.

Claims 10-12 (Canceled)

13. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has V_L comprising the amino acid sequence of

X₁X₂X₃X₄TQX₅PSX₆X₇SX₈X₉X₁₀GX₁₁X₁₂X₁₃X₁₄IX₁₅CX₁₆X₁₇SX₁₈X₁₉IX₂₀X₂₁X₂
X₂₃X₂₄WYQQX₂₅PGX₂₆APX₂₇X₂₈LX₂₉YX₃₀X₃₁X₃₂X₃₃LX₃₄X₃₅GVX₃₆X₃₇RFSGX₃₈X₃₉SGT
DFX₄₀LТИX₄₁X₄₂LQX₄₃X₄₄DX₄₅AX₄₆YYCQQX₄₇X₄₈X₄₉X₅₀PX₅₁TFGX₅₂GTKX₅₃X₅₄IK,
wherein the underlined regions are designated as V_L/CDR1, V_L/CDR2, and V_L/CDR3, respectively, whereas the rest of the region is designated as framework, and wherein X₁ is D, E or A; X₂ is I, or T; X₃ is V, E, K, R, Q, or T; X₄ is M, or L; X₅ is S, or T, X₆ is S, or T; X₇ is L, or V; X₈ is A, or V; X₉ is S, or T; X₁₀ is P, V, L, A, or I; X₁₁ is E, or D; X₁₂ is R, or T; X₁₃ is A, or V I; X₁₄ is T, or A; X₁₅ is T, S, or A; X₁₆ is S, R, N, K, H, or Q; X₁₇ is A, or S; X₁₈ is Q, or R; X₁₉ is S, D, A, or P; X₂₀ is S, G, R, T, or Y; X₂₁ is T, N, S, D, or K; X₂₂ is Y, or D; X₂₃ is L, or I; X₂₄ is A, N, or T; X₂₅ is K, or I; X₂₆ is Q, K, T, or I; X₂₇ is R, K, Q, N, H, S, or E; X₂₈ is V, or L; X₂₉ is I, or V; X₃₀ is F, A, G, D, or S; X₃₁ is A, or T; X₃₂ is S, or T; X₃₃ is N, S, R, or T; X₃₄ is A, H, or Q; X₃₅ is S, or G; X₃₆ is P, T; X₃₇ is S, N, D, G, or Y; X₃₈ is S, or T; X₃₉ is G, or R; X₄₀ is T, or A; X₄₁ is S, or R; X₄₂ is S, or R; X₄₃ is P, or A; X₄₄

is E , or D; X₄₅ is F, V, or S; X₄₆ is V, T, I , or S; X₄₇ is Y, or S; X₄₈ is S, Y, or N; X₄₉ is S , or T; X₅₀ is T, V, A, P, K, G, S, or I; X₅₁ is W , or Y; X₅₂ is Q , or G; X₅₃ is V, or L; and X₅₄ is E, D , or A.

14. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has V_L comprising the amino acid sequence of

X₁X₂X₃LTQPPSX₄SX₅TPGQX₆VTISCSGX₇X₈SNX₉GX₁₀NX₁₁VX₁₂WYQQX₁₃P
GX₁₄APKX₁₅LX₁₆YX₁₇NX₁₈X₁₉RPSGVPX₂₀RX₂₁SGSX₂₂SX₂₃TSASLAISGLX₂₄SEDEADY
YCX₂₅X₂₆WDDSLX₂₇GYVFGX₂₈GTX₂₉LTVL, wherein the underlined regions are designated as V_L/CDR1, V_L/CDR2, and V_L/CDR3, respectively, whereas the rest of the region is designated as framework, and wherein X₁ is Q L, or N; X₂ is P A F, or S; X₃ is V, or M; X₄ is A, or T; X₅ is G, or A; X₆ is R, or S; X₇ is S, or T; X₈ is S, T Y, or N; X₉ is I , or V; X₁₀ is S, or R; X₁₁ is S, P, N, A, or T; X₁₂ is N, T , or Y; X₁₃ is L, or F; X₁₄ is T, or A; X₁₅ is V, L, or F; X₁₆ is M, or I; X₁₇ is G, T, or S; X₁₈ is N, or D; X₁₉ is Q, or E; X₂₀ is D, or E; X₂₁ is F, or L; X₂₂ is K, or R; X₂₃ is G, or A; X₂₄ is Q, L, or R; X₂₅ is A, or G; X₂₆ is A, S, or T; X₂₇ is N, S, or T; X₂₈ is T, or A; and X₂₉ is K, or Q.

15. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has V_L comprising the amino acid sequence of

QSALTQPPSVSGAPGQRVTISCTGRSSNIGAGHDVHWYQQLPGTAPKLLIY
ANDQRPSGVPDFSDSKSGTSASLGISGLRSEDEADYFCATWDDSLHGYVFGTGTKV
TVL (SEQ ID No: 54).

16. (Withdrawn) A monoclonal antibody is provided that specifically binds to a human VEGF and has V_H comprising the amino acid sequence of

X₁X₂QLVX₃SGGGX₄VQPGGX₅LRLX₆CAX₇SGX₈X₉X₁₀X₁₁X₁₂X₁₃GX₁₄NWX₁₅
RQAPGKGX₁₆EWVGWX₁₇NTX₁₈X₁₉GX₂₀X₂₁TYX₂₂X₂₃X₂₄FX₂₅RRX₂₆TX₂₇SX₂₈X₂₉X₃₀SK
X₃₁X₃₂X₃₃YLQX₃₄NSLRAEDTAVYYCAX₃₅YPX₃₆YYGX₃₇SHWYFDVWX₃₈QGTLVTVS
S, wherein the underlined regions are designated as CDR1, CDR2, and CDR3, respectively, whereas the rest of the region is designated as framework according to Kabat nomenclature, and wherein X₁ is E, or Q; X₂ is V, or G; X₃ is Q, or E; X₄ is V, or L; X₅ is S, or T; X₆ is S T, or R; X₇ is A, or V; X₈ is Y, or F; X₉ is T, D, N, S, or A; X₁₀ is F, or L; X₁₁ is T, D, Y, A, S, or N; X₁₂ is N, H, or S; X₁₃ is Y, or F; X₁₄ is M, L, I, or V; X₁₅ is I, V, or L; X₁₆ is L, or P;

X₁₇ is I, or V; X₁₈ is Y, or N; X₁₉ is T, or N; X₂₀ is E, or A; X₂₁ is P, T, or S; X₂₂ is A, or V; X₂₃ is A, H, Q, P, D, or E; X₂₄ is D, or E; X₂₅ is K, or T; X₂₆ is V, F, or L; X₂₇ is F, or I; X₂₈ is L, or R; X₂₉ is D, or N; X₃₀ is T, or N; X₃₁ is S, or N; X₃₂ is T, Q, P, or K; X₃₃ is A, V, or P; X₃₄ is L, or M; X₃₅ is K, or R; X₃₆ is H, or Y; X₃₇ is S, R, or T; and X₃₈ is G, or A.

17. (Withdrawn) A monoclonal antibody is provided that specifically binds to a human VEGF and has V_L comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:2-54, more preferably comprising the amino acid sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:44, SEQ ID NO:47, and SEQ ID NO:54.

18. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has V_H comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:57-110 and SEQ ID NOs:285-310, and preferably comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:61-64, SEQ ID NO:67, 68, 70, 75, 83, 88, 89, 90, 91, 92, 93, 94, and 96-110.

19. (Withdrawn) A monoclonal antibody is provided that specifically binds to a human VEGF and has CDR2 in the V_L region (V_L/CDR2) comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:195-209.

20. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has CDR3 in the V_L region (V_L/CDR3) comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:210-228.

21. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has a framework region (FR) CDR3 in the V_L region (V_L/FR) comprising the amino acid sequence selected from the group consisting of: SEQ ID NO:229-269, and preferably comprising the amino acid sequence selected from the group consisting of SEQ ID NO:232, 235, 237, 251, 255, 263, and 265.

22. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has CDR1 in the V_H region (V_H/CDR1) comprising the amino acid sequence of

$\text{GX}_1\text{X}_2\text{X}_3\text{X}_4\text{X}_5\text{X}_6\text{GX}_7\text{N}$, wherein X_1 is Y, or F; X_2 is D, N, T, S, or A; X_3 is F, or L; X_4 is T, D, S, Y, A, or N; X_5 is H, N, or S; X_6 is Y, or F; X_7 is M, L, I, or V.

23. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has CDR2 in the V_H region (V_H /CDR2) comprising the amino acid sequence of $\text{WX}_1\text{NTX}_2\text{X}_3\text{GEX}_4\text{TYX}_5\text{X}_6\text{X}_7\text{FX}_8\text{R}$, wherein X_1 is I, or V; X_2 is Y, or N; X_3 is T, or N; X_4 is P, T, or S; X_5 is A, or V; X_6 is A, Q, P, H, D, or E; X_7 is D, or E; and X_8 is K, or T.

24. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has CDR2 in the V_H region (V_H /CDR2) comprising the amino acid sequence selected from the group consisting of: SEQ ID NOs:136-156.

25. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has CDR3 in the V_H region (V_H /CDR3) comprising the amino acid sequence of $\text{KYPX}_1\text{YYGX}_2\text{SHWYFDV}$, wherein X_1 is Y, or H, and X_2 is R.

26. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has CDR3 in the V_H region (V_H /CDR3) comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:311-337.

27. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has FR in the V_H region (V_H /FR) comprising the amino acid sequence of $\text{X}_1\text{VQLVX}_2\text{SGGGX}_3\text{VQPGGX}_4\text{LRLX}_5\text{CAX}_6\text{S}/\text{CDR1/WX}_7\text{RQAPGKGLEWVG/CDR2/RX}_8\text{TX}_9\text{SX}_10\text{DX}_11\text{SKX}_12\text{X}_13\text{X}_14\text{YLQX}_15\text{NSLRAEDTAVYYCA/CDR3/WX}_16\text{QGTLVTVSS}$, wherein X_1 is E, or Q; X_2 is Q, or E; X_3 is V, or L; X_4 is S, or T; X_5 is S, T, or R; X_6 is A, or V; X_7 is I, or V; X_8 is F, or V; X_9 is F, or I; X_{10} is L, or R is X_{11} is T, or N; X_{12} is S, or N; X_{13} is T, Q, or K; X_{14} is A, or V; X_{15} is M, or L; and X_{16} is G, or A.

28. (Previously Presented) A monoclonal antibody that specifically binds to a human VEGF and has a V_L and V_H pair selected from the group consisting of: SEQ ID NO:28 and 88; SEQ ID NO:28 and 90; SEQ ID NO:28 and 91; SEQ ID NO:28 and 106; SEQ ID NO:28 and 107; SEQ ID NO:28 and 108; and SEQ ID NO:28 and 109.

29. (Withdrawn) The monoclonal antibody of any of claims 14-29, wherein the antibody has dissociation constant K_d equal to or lower than 10 nM.

30. (Withdrawn) The monoclonal antibody of any of claims 14-29, wherein the antibody has dissociation constant K_d equal to or lower than 1 nM.

31. (Withdrawn) The monoclonal antibody of any of claims 14-29, wherein the antibody has dissociation constant K_d equal to or lower than 0.1 nM.

32. (Withdrawn) The monoclonal antibody of any of claims 14-29, wherein the antibody has dissociation constant K_d equal to or lower than 0.01 nM.

33. (Previously presented) A monoclonal antibody that specifically binds to human VEGF and has a VL and VH pair selected from the group consisting of: SEQ ID NO:26 and 88; SEQ ID NO:26 and 90; SEQ ID NO:26 and 91; SEQ ID NO:26 and 106; SEQ ID NO:26 and 107; SEQ ID NO:26 and 108; SEQ ID NO:26 and 109; SEQ ID NO:28 and 88; SEQ ID NO:28 and 90; SEQ ID NO:28 and 91; SEQ ID NO:28 and 106; SEQ ID NO:28 and 107; SEQ ID NO:28 and 108; SEQ ID NO:28 and 109; SEQ ID NO:36 and 88; SEQ ID NO:36 and 90; SEQ ID NO:36 and 91; SEQ ID NO:36 and 106; SEQ ID NO:36 and 107; SEQ ID NO:36 and 108; and SEQ ID NO:36 and 109.

34. (Previously presented) A monoclonal antibody that specifically binds to human VEGF and has a VL and VH pair selected from the group consisting of: SEQ ID NO:26 and 106; SEQ ID NO:28 and 106; and SEQ ID NO:36 and 106.

35. (Previously presented) A monoclonal antibody that specifically binds to human VEGF and has a V_L and V_H pair consisting of SEQ ID NO:28 and 106.

36. (Previously presented) A monoclonal antibody that specifically binds to human VEGF and has a VL domain consisting of SEQ ID NO:28 in combination with a VH domain selected from SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO:108, SEQ ID NO: 109, SEQ ID NO: 88, SEQ ID NO: 90, and SEQ ID NO: 91 .

37. (Previously presented) The monoclonal antibody of claim 35, wherein the antibody is a scFv.

38. (Previously presented) The monoclonal antibody of claim 35, wherein the antibody is a Fab.

39. (Previously presented) The monoclonal antibody of claim 35, wherein the antibody is a fully assembled antibody.

40. (Currently amended) A ~~monoclonal recombinant~~ antibody that specifically binds to [[a]] human VEGF and has a light chain variable domain (V_L) comprising CDR1, CDR2 and CDR3 regions consisting of the amino acid sequences set forth in SEQ ID NO: 172, SEQ ID NO: 195 and SEQ ID NO: 212, respectively.

41. (Currently amended) The ~~monoclonal recombinant~~ antibody according to claim 40, wherein the heavy chain variable domain (V_H) comprises CDR1, CDR2, and CDR3 regions consisting of the amino acid sequences set forth in SEQ ID NO: 31, SEQ ID NO: 152 and SEQ ID NO: 327, respectively.

42. (Currently amended) The ~~monoclonal recombinant~~ antibody of claim 41, wherein the antibody is a scFv.

43. (Currently amended) The ~~monoclonal recombinant~~ antibody of claim 41, wherein the antibody is a Fab.

44. (Currently amended) The ~~monoclonal recombinant~~ antibody of claim 41, wherein the antibody is a fully assembled antibody.

45. (Currently amended) A ~~monoclonal recombinant~~ antibody that specifically binds to [[a]] human VEGF and has a V_L domain comprising CDR1, CDR2 and CDR3 regions consisting of the amino acid sequences set forth in SEQ ID NO: 170, SEQ ID NO: 195 and SEQ ID NO: 214, respectively.

46. (Currently amended) A monoclonal recombinant antibody that specifically binds to [[a]] human VEGF and has a ~~heavy chain variable~~ V_H domain ~~which comprises~~ comprising CDR1, CDR2, and CDR3 regions consisting of the amino acid sequences set forth in SEQ ID NO: 31, SEQ ID NO: 152 and SEQ ID NO: 327, respectively.

47. (Currently amended) A monoclonal recombinant antibody that specifically binds to [[a]] human VEGF and has V_L comprising CDR1, CDR2 and CDR3 regions consisting of the amino acid sequences set forth in SEQ ID NO: 182, SEQ ID NO: 201 and SEQ ID NO: 222, respectively.

48. (Previously presented) An antibody heavy chain variable domain (VH) consisting of an amino acid sequence selected from SEQ ID NO: 88, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 106, SEQ ID NO:107, SEQ ID NO: 108 and SEQ ID NO:109.

49. (Previously presented) An antibody light chain variable domain (VL) consisting of an amino acid sequence selected from SEQ ID NO: 26, SEQ ID NO: 28, and SEQ ID NO:36.